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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,612	05/14/2001	Thomas Spies	FHCC:003USC1	9260

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EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/855,612	SPIES ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 09/303,161, which claims the benefit of the filing date of provisional application 60/029,044.

Claims 26-101 have been canceled.

Claims 1-25 are currently pending and are the subject of examination in the present Office Action.

In view of Applicant's response filed June 16, 2003, all previous grounds of rejection are withdrawn.

The following represent new grounds of rejection and this Office Action is made Non-Final.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-25 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It was previously stated: "Briefly, claims 1-25 are drawn to a method of detecting a cancer cell in a sample comprising detecting a cancer cell in a sample. Said method encompasses MICA or MICB binding agents, wherein said binding agent is an antibody that can be labeled or can be bound by a second antibody, which in turn can be labeled. Said method also encompasses amplifying a MICA or MICB transcript.

The specification discloses on page 9 that the "inventors have shown that MICA is expressed in various cancer cell lines suggesting that cells may be screened for the overexpression of MICA and/or MICB, its presence indicating potential carcinogenesis." The specification further discloses that the "expression of MICA in tumor cells provides a marker for diagnostic screening methods for cancer in, for example, tumor or tissue biopsy samples" (page 10, lines 4-5), and that "MICA and/or MICB expression in tumor cells may be detected" (page 10, lines 5-6). The specification also discloses on page 75, lines 1-9 that MICA was detected on tumor cell lines HT29 (colon carcinoma) and U373 (astrocytoma).

However, the specification does not disclose how to correlate the level of MICA/B expression in a sample to the presence of cancer versus the level of MICA/B expression in normal tissue or due to other factors. Groh et al (PNAS 93:12445-12450; of record) teaches that MICA and MICB are normally expressed in the gastrointestinal epithelium but does not indicate expression associated with cancer cells

(see entire article, Abstract in particular). Groh et al (Science 1998 279:1737-1740; U on form PTO-892) discloses expression of MICA and MICB is stress related and may be indicative of damaged, infected or transformed intestinal epithelial cells (see entire report, page 1740 in particular).

Given that the state of the art at the time the invention was made does not appear to teach the expression of MICA or MICB solely in association with cancer cells, the artisan would not have been able to predict that the mere detection of MICA and/or MICB in a sample would be indicative of cancer as opposed to being present normally or due to some other form of stress on the originating tissue or organism of the sample. The instant disclosure provides limited guidance in the specification regarding a method for the artisan to detect a cancer cell in a sample comprising identifying expression of MICA or MICB in said sample without correlation of that expression level to the expression level in normal tissue or samples which may exhibit stress induced expression of MICA and/or MICB.

Given the limited working examples in the specification, the state of the art at the time the invention was made and the level of guidance required to practice the claimed invention, it would require undue experimentation for one of skill to predict which if any types of cancer cells could be detected in a sample comprising identifying expression of MICA or MICB in said sample, without further guidance from the specification."

Applicant's arguments and the joint declaration of inventors Thomas Spies & Veronica Spies filed January 12, 2004 have been fully considered but they are not persuasive.

Applicant asserts that the claims are enabled for the diagnosis of a plurality of cancers. Applicant asserts in the Declaration and contends in the response that because MICA and MICB are expressed on the surface of colon and other cancer cells, that mere detection of MICA and MICB in samples suspected of having cancer cells "could be indicative of cancer." The Examiner does not question the veracity of Applicant's statement that MICA and MICB detection in a tissue sample may be indicative of cancer. However, the fact remains that the prior art discloses that some normal tissues, including intestinal epithelium, and tissues under stress from causes not related to cancer can also express MICA and MICB. Applicant asserts that a demonstration was made that MICA and MICB were detectable in colon cancer samples. However, given that Groh et al (PNAS 93:12445-12450; of record) teaches that MICA and MICB are normally expressed in the gastrointestinal epithelium, simple detection of MICA and MICB can also occur in normal tissue samples. Mere detection of MICA and/or MICB in a tissue sample is insufficient as an indicator of cancer in the sample or the subject from whom the sample is obtained. Therefore, at what point does MICA and MICB detection in the tissue become indicative of cancer? If indicators that are present in normal tissue are to be used as an indicator of diseased, cancerous tissue, there must exist a means for differentiating the expression of those indicators in the cancerous tissue from the expression of those indicators in the normal tissue. Accordingly, the invention as presently claimed is not enabled because it does not provide a means for differentiating cancerous samples from normal tissue or non-cancerous stressed tissue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-25 stand rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are:

It was previously stated: "Correlation of the level of MICA or MICB expression in the sample to the presence of cancer.

The claims are drawn to a diagnostic method in which the level of MICA and/or MICB expression is used to detect a cancer cell in a sample. However, MICA and MICB are MHC-related stress proteins that are also expressed under conditions of stress other than cancer, as well as on normal intestinal epithelial cells. Accordingly, in order to make a determination of cancer, the level of expression in a sample must be contrasted to expression under normal or stress conditions."

Applicant argues that no steps are missing in the claimed method for the same reasons that Applicant asserts the claimed invention is enabled. However, for the reasons stated supra in response to Applicant's arguments, the claims still lack a step that differentiates between normal and cancerous tissue.

Conclusion

4. No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
April 1, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
4/5/04